PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 18062G-48-1P	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/17281	International filing date *(day/month/year)* 30 May 2003 (30.05.2003)	Priority date *(day/month/year)* 31 May 2002 (31.05.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 9/127 and US Cl.: 424/450		
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23 December 2003 (23.12.2003)	20 September 2004 (20.09.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Richard Schnizer, Ph. D Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY [redacted]AMINATION REPORT

International applicatio[redacted]
PCT/US03/17281

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-26 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 27-33, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-6, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY [redacted]MINATION REPORT

International application [redacted]
PCT/US03/17281

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-19, 25-41	YES
	Claims 20-24	NO
Inventive Step (IS)	Claims 10, 18, 19, 25, 33, 41	YES
	Claims 1-9, 11-17, 20-24, 26-32, 34-40	NO
Industrial Applicability (IA)	Claims 1-41	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 20-24 lack novelty under PCT Article 33(2) as being anticipated by Lizarzaburu et al (1999).

Lizarzaburu taught tetraester polyamine lipids for gene transfection that are identical to formula 1 wherein R1 and R2 are C13 alkyl or C17 alkene, R3 and R4 are H, m and n are 1 or 2, and Y1-4 are CH3.

Claims 1, 2, 5-13, 26-30, 34-38 lack an inventive step under PCT Article 33(3) as being obvious over Lizarzaburu et al (1999).

Lizarzaburu taught tetraester polyamine lipids for gene transfection that are identical to formula 1 wherein R1 and R2 are C13 alkyl or C17 alkene, R3 and R4 are H, m and n are 1 or 2, and Y1-4 are CH3.

Lizarzaburu did not teach a lipoplex between the lipids and a nucleic acid, or the use of the lipids to deliver DNA to tissue, but it would have been obvious to use the lipids for these purposes because Lizarzaburu suggests that the lipids are intended to solve gene delivery problems in gene therapy. It would have been similarly obvious to compare the efficiency of the different lipids in gene delivery. It would also have been obvious to vary the lengths of the alkyl or alkenyl chains in the process of optimizing the performance of the lipids.

Claims 3, 4, 14-17, 31, 32, 39, and 40 lack an inventive step under PCT Article 33(3) as being obvious over Lizarzaburu et al (1999)in view of Kolbe et al (2002).

Lizarzaburu taught tetraester polyamine lipids for gene transfection that are identical to formula 1 wherein R1 and R2 are C13 alkyl or C17 alkene, R3 and R4 are H, m and n are 1 or 2, and Y1-4 are CH3.

Lizarzaburu did not teach a target tissue of tumor, organ, or bone, nor specific N/P ratios, nor plasmid DNA or antisense DNA or RNA.

Kolbe taught the use of cationic molecules for condensation of nucleic acids for delivery to cells. Kolbe taught that plasmid DNA or antisense DNA or RNA could be delivered to cancer cells, organs, and bone, and that the N/P ratio was a result-effective variable that should be varied in order to optimize success. Specifically Kolbe taught that N/P should be between 2.5 and 5. As such it would have been obvious to use the cationic lipids of Lizarzaburu to deliver plasmid DNA or antisense DNA or RNA to cancer cells, organs, or bone, and to optimize the N/P ratio.

---------- NEW CITATIONS ----------

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 10, 25, 33, and 41 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claimed strucures are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: the claims are drawn to quaternary amine salts of the compounds of formula 1, but the compounds of formula 1 comprise only secondary and tertiary amines, and do not allow for any quaternary amines.